



SEQUENCE LISTING

<110> OXVIG, Claus
OVERGAARD, Michael T.

<120> PREGNANCY-ASSOCIATED PLASMA PROTEIN-A2 (PAPP-A2)

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<140> US 09/983,025
<141> 2001-10-22

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<151> 2000-10-20

<150> DK PA 2000 01571
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<170> Patent in version 3.1

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Met Tyr Glu Gly Asp Gly Ile Cys Glu Pro Phe Glu Arg Lys Thr Ser	
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Ile Val Asp Cys Gly Ile Tyr Thr Pro Lys Gly Tyr Leu Asp Gln Trp	
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Trp	His	Pro	Asp	Pro	Val	Leu	Val	His	Cys	Ile	Gln	Ser	Cys	Glu	
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Tyr	Cys	His	Tyr	Asp	Gly	Gly	Asp	Cys	Cys	Ser	Ser	Thr	Leu	Ser	
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Ser	Lys	Lys	Val	Ile	Pro	Phe	Ala	Ala	Asp	Cys	Asp	Leu	Asp	Glu	
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Ala Val Glu Glu Pro Ala Ala Pro Trp Val Gly Asp Ser Pro Ile
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Arg Ser Lys Glu Ser Leu Gly Glu Ala Gly Ile Gln Lys Gly Ser Ala
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Gln Val Trp Lys Arg Arg Ala Glu Asp Gly Gln Gly Asp Ser Gly Ile
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Lys Lys Ser Pro Pro Glu Glu Ser Asn Gln Asn Gly Gly Glu Gly Ser
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Tyr Phe Ser Gly Arg Arg Glu Arg Leu Leu Leu Arg Pro Glu Val Leu
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Ala Glu Ile Pro Arg Glu Ala Phe Thr Val Glu Ala Trp Val Lys Pro
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Glu Gly Gly Gln Asn Asn Pro Ala Ile Ile Ala Gly Val Phe Asp Asn
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Cys Ser His Thr Val Ser Asp Lys Gly Trp Ala Leu Gly Ile Arg Ser
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Gly Lys Asp Lys Gly Lys Arg Asp Ala Arg Phe Phe Phe Ser Leu Cys
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Thr Asp Arg Val Lys Lys Ala Thr Ile Leu Ile Ser His Ser Arg Tyr
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Gln Pro Gly Thr Trp Thr His Val Ala Ala Thr Tyr Asp Gly Arg His
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His Ser Ser Gln His Ser Ser Gly Glu Glu Glu Ala Thr Asp Leu Val
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Ser Val His Gln Val His Asn Ser Thr Leu Arg His Arg Val Val Leu
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Val Asn Cys Glu Pro Ser Lys Ile Gly Asn Asp His Cys Asp Pro Glu
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Cys Glu His Pro Leu Thr Gly Tyr Asp Gly Gly Asp Cys Arg Leu Gln
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Gly Arg Cys Tyr Ser Trp Asn Arg Arg Asp Gly Leu Cys His Val Glu
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480 485 490

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Val Phe Lys Gly Val Ser Glu Arg Glu Ser Cys Asn Asp Pro Cys Lys
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Glu Thr Val Pro Ser Met Glu Thr Gly Asp Leu Cys Ala Asp Thr Ala
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Pro Thr Pro Lys Ser Glu Leu Cys Arg Glu Pro Glu Pro Thr Ser Asp
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Thr Cys Gly Phe Thr Arg Phe Pro Gly Ala Pro Phe Thr Asn Tyr Met
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575 580 585 590

Ala Arg Met His Cys Tyr Leu Asp Leu Val Tyr Gln Gln Trp Thr Glu
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625 630 635

Val Tyr Asp Arg Ala Ser Gly Ser Leu Cys Gly Ala Cys Thr Glu Asp
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Gly	Leu	Pro	Val	Val	Val	Thr	His	Ser	His	Arg	Lys	Phe	Thr	Asp	Val	835	840	845	
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Ala Pro Tyr Cys Gly Asp Gly Lys Val Ser Glu Arg Leu Gly Glu Glu
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His Gln Asn Val Leu Phe His His Thr Thr Ser Val Leu Leu Asn
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Ala	Ile	Thr	Cys	Gln	Arg	Gly	Phe	Ala	Leu	Gln	Ala	Ser	Ser	Gly
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Asn Ser Ala Val Asp
1 5

<210> 21

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> primer containing XhoI site, for amplifying IGFBP-5 cDNA

<400> 21

tccgctcgag atggtgttgc tcaccgcggt

30

<210> 22

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> primer containing HindIII site, for amplifying IGFBP-5 cDNA

<400> 22

cgataagctt ctcaacgttg ctgctgtcg

29

<210> 23
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> N-terminal sequence of degradation product of purified rIGFBP-5
 digested with PAPP-A2

<400> 23

Lys Phe Val Gly Gly Ala
 1 5

<210> 24
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
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 digested with PAPP-A2

<220>
 <221> misc_feature
 <222> (3)..(3)
 <223> Xaa is unknown

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 1 5

<210> 25
 <211> 1627
 <212> PRT
 <213> Homo sapiens

<400> 25

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Leu Gly Cys Gly Leu Ala Glu Arg Pro Arg Arg Ala Arg Arg Asp Pro
 20 25 30

Arg Ala Gly Arg Pro Pro Arg Pro Ala Ala Gly Pro Ala Thr Cys Ala
 35 40 45

Thr Arg Gly Pro Arg Pro Pro Arg Leu Ala Ala Ala Ala Ala Ala
 50 55 60

Gly Arg Ala Trp Glu Ala Val Arg Val Pro Arg Arg Arg Gln Gln Arg
65 70 75 80

Glu Ala Arg Gly Ala Thr Glu Glu Pro Ser Pro Pro Ser Arg Ala Leu
85 90 95

Tyr Phe Ser Gly Arg Gly Glu Gln Leu Arg Val Leu Arg Ala Asp Leu
100 105 110

Glu Leu Pro Arg Asp Ala Phe Thr Leu Gln Val Trp Leu Arg Ala Glu
115 120 125

Gly Gly Gln Arg Ser Pro Ala Val Ile Thr Gly Leu Tyr Asp Lys Cys
130 135 140

Ser Tyr Ile Ser Arg Asp Arg Gly Trp Val Val Gly Ile His Thr Ile
145 150 155 160

Ser Asp Gln Asp Asn Lys Asp Pro Arg Tyr Phe Phe Ser Leu Lys Thr
165 170 175

Asp Arg Ala Arg Gln Val Thr Thr Ile Asn Ala His Arg Ser Tyr Leu
180 185 190

Pro Gly Gln Trp Val Tyr Leu Ala Ala Thr Tyr Asp Gly Gln Phe Met
195 200 205

Lys Leu Tyr Val Asn Gly Ala Gln Val Ala Thr Ser Gly Glu Gln Val
210 215 220

Gly Gly Ile Phe Ser Pro Leu Thr Gln Lys Cys Lys Val Leu Met Leu
225 230 235 240

Gly Gly Ser Ala Leu Asn His Asn Tyr Arg Gly Tyr Ile Glu His Phe
245 250 255

Ser Leu Trp Lys Val Ala Arg Thr Gln Arg Glu Ile Leu Ser Asp Met
260 265 270

Glu Thr His Gly Ala His Thr Ala Leu Pro Gln Leu Leu Leu Gln Glu
275 280 285

Asn Trp Asp Asn Val Lys His Ala Trp Ser Pro Met Lys Asp Gly Ser

290		295		300											
Ser 305	Pro	Lys	Val	Glu	Phe 310	Ser	Asn	Ala	His	Gly 315	Phe	Leu	Leu	Asp	Thr 320
Ser	Leu	Glu	Pro	Pro 325	Leu	Cys	Gly	Gln	Thr 330	Leu	Cys	Asp	Asn	Thr 335	Glu
Val	Ile	Ala	Ser 340	Tyr	Asn	Gln	Leu	Ser 345	Ser	Phe	Arg	Gln	Pro 350	Lys	Val
Val	Arg	Tyr 355	Arg	Val	Val	Asn	Leu 360	Tyr	Glu	Asp	Asp	His 365	Lys	Asn	Pro
Thr 370	Val	Thr	Arg	Glu	Gln	Val 375	Asp	Phe	Gln	His	His 380	Gln	Leu	Ala	Glu
Ala 385	Phe	Lys	Gln	Tyr	Asn 390	Ile	Ser	Trp	Glu	Leu 395	Asp	Val	Leu	Glu	Val 400
Ser	Asn	Ser	Ser	Leu 405	Arg	Arg	Arg	Leu	Ile 410	Leu	Ala	Asn	Cys	Asp 415	Ile
Ser	Lys	Ile	Gly 420	Asp	Glu	Asn	Cys	Asp 425	Pro	Glu	Cys	Asn	His 430	Thr	Leu
Thr	Gly 435	His	Asp	Gly	Gly	Asp 440	Cys	Arg	His	Leu	Arg	His 445	Pro	Ala	Phe
Val 450	Lys	Lys	Gln	His	Asn	Gly 455	Val	Cys	Asp	Met	Asp 460	Cys	Asn	Tyr	Glu
Arg 465	Phe	Asn	Phe	Asp	Gly 470	Gly	Glu	Cys	Cys	Asp 475	Pro	Glu	Ile	Thr	Asn 480
Val	Thr	Gln	Thr	Cys 485	Phe	Asp	Pro	Asp	Ser 490	Pro	His	Arg	Ala	Tyr 495	Leu
Asp	Val	Asn	Glu 500	Leu	Lys	Asn	Ile	Leu 505	Lys	Leu	Asp	Gly	Ser 510	Thr	His
Leu	Asn 515	Ile	Phe	Phe	Ala	Lys	Ser 520	Ser	Glu	Glu	Glu	Leu 525	Ala	Gly	Val

Ala Thr Trp Pro Trp Asp Lys Glu Ala Leu Met His Leu Gly Gly Ile
 530 535 540

Val Leu Asn Pro Ser Phe Tyr Gly Met Pro Gly His Thr His Thr Met
 545 550 555 560

Ile His Glu Ile Gly His Ser Leu Gly Leu Tyr His Val Phe Arg Gly
 565 570 575

Ile Ser Glu Ile Gln Ser Cys Ser Asp Pro Cys Met Glu Thr Glu Pro
 580 585 590

Ser Phe Glu Thr Gly Asp Leu Cys Asn Asp Thr Asn Pro Ala Pro Lys
 595 600 605

His Lys Ser Cys Gly Asp Pro Gly Pro Gly Asn Asp Thr Cys Gly Phe
 610 615 620

His Ser Phe Phe Asn Thr Pro Tyr Asn Asn Phe Met Ser Tyr Ala Asp
 625 630 635 640

Asp Asp Cys Thr Asp Ser Phe Thr Pro Asn Gln Val Ala Arg Met His
 645 650 655

Cys Tyr Leu Asp Leu Val Tyr Gln Gly Trp Gln Pro Ser Arg Lys Pro
 660 665 670

Ala Pro Val Ala Leu Ala Pro Gln Val Leu Gly His Thr Thr Asp Ser
 675 680 685

Val Thr Leu Glu Trp Phe Pro Pro Ile Asp Gly His Phe Phe Glu Arg
 690 695 700

Glu Leu Gly Ser Ala Cys His Leu Cys Leu Glu Gly Arg Ile Leu Val
 705 710 715 720

Gln Tyr Ala Ser Asn Ala Ser Ser Pro Met Pro Cys Ser Pro Ser Gly
 725 730 735

His Trp Ser Pro Arg Glu Ala Glu Gly His Pro Asp Val Glu Gln Pro
 740 745 750

Cys Lys Ser Ser Val Arg Thr Trp Ser Pro Asn Ser Ala Val Asn Pro

755

760

765

His Thr Val Pro Pro Ala Cys Pro Glu Pro Gln Gly Cys Tyr Leu Glu
770 775 780

Leu Glu Phe Leu Tyr Pro Leu Val Pro Glu Ser Leu Thr Ile Trp Val
785 790 795 800

Thr Phe Val Ser Thr Asp Trp Asp Ser Ser Gly Ala Val Asn Asp Ile
805 810 815

Lys Leu Leu Ala Val Ser Gly Lys Asn Ile Ser Leu Gly Pro Gln Asn
820 825 830

Val Phe Cys Asp Val Pro Leu Thr Ile Arg Leu Trp Asp Val Gly Glu
835 840 845

----- Glu Val Tyr Gly Ile Gln Ile Tyr Thr Leu Asp Glu His Leu Glu Ile
850 855 860

Asp Ala Ala Met Leu Thr Ser Thr Ala Asp Thr Pro Leu Cys Leu Gln
865 870 875 880

Cys Lys Pro Leu Lys Tyr Lys Val Val Arg Asp Pro Pro Leu Gln Met
885 890 895

Asp Val Ala Ser Ile Leu His Leu Asn Arg Lys Phe Val Asp Met Asp
900 905 910

Leu Asn Leu Gly Ser Val Tyr Gln Tyr Trp Val Ile Thr Ile Ser Gly
915 920 925

Thr Glu Glu Ser Glu Pro Ser Pro Ala Val Thr Tyr Ile His Gly Arg
930 935 940

Gly Tyr Cys Gly Asp Gly Ile Ile Gln Lys Asp Gln Gly Glu Gln Cys
945 950 955 960

Asp Asp Met Asn Lys Ile Asn Gly Asp Gly Cys Ser Leu Phe Cys Arg
965 970 975

Gln Glu Val Ser Phe Asn Cys Ile Asp Glu Pro Ser Arg Cys Tyr Phe
980 985 990

His Asp Gly Asp Gly Val Cys Glu Glu Phe Glu Gln Lys Thr Ser Ile
 995 1000 1005

Lys Asp Cys Gly Val Tyr Thr Pro Gln Gly Phe Leu Asp Gln Trp
 1010 1015 1020

Ala Ser Asn Ala Ser Val Ser His Gln Asp Gln Gln Cys Pro Gly
 1025 1030 1035

Trp Val Ile Ile Gly Gln Pro Ala Ala Ser Gln Val Cys Arg Thr
 1040 1045 1050

Lys Val Ile Asp Leu Ser Glu Gly Ile Ser Gln His Ala Trp Tyr
 1055 1060 1065

Pro Cys Thr Ile Ser Tyr Pro Tyr Ser Gln Leu Ala Gln Thr Thr
 1070 1075 1080

Phe Trp Leu Arg Ala Tyr Phe Ser Gln Pro Met Val Ala Ala Ala
 1085 1090 1095

Val Ile Val His Leu Val Thr Asp Gly Thr Tyr Tyr Gly Asp Gln
 1100 1105 1110

Lys Gln Glu Thr Ile Ser Val Gln Leu Leu Asp Thr Lys Asp Gln
 1115 1120 1125

Ser His Asp Leu Gly Leu His Val Leu Ser Cys Arg Asn Asn Pro
 1130 1135 1140

Leu Ile Ile Pro Val Val His Asp Leu Ser Gln Pro Phe Tyr His
 1145 1150 1155

Ser Gln Ala Val Arg Val Ser Phe Ser Ser Pro Leu Val Ala Ile
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Ser Gly Val Ala Leu Arg Ser Phe Asp Asn Phe Asp Pro Val Thr
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Leu Ser Ser Cys Gln Arg Gly Glu Thr Tyr Ser Pro Ala Glu Gln
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Ser Cys Val His Phe Ala Cys Glu Lys Thr Asp Cys Pro Glu Leu

1205		1210		1215
Ala Val Glu Asn Ala Ser Leu Asn Cys Ser Ser Ser Asp Arg Tyr				
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His Gly Ala Gln Cys Thr Val Ser Cys Arg Thr Gly Tyr Val Leu				
1235		1240		1245
Gln Ile Arg Arg Asp Asp Glu Leu Ile Lys Ser Gln Thr Gly Pro				
1250		1255		1260
Ser Val Thr Val Thr Cys Thr Glu Gly Lys Trp Asn Lys Gln Val				
1265		1270		1275
Ala Cys Glu Pro Val Asp Cys Ser Ile Pro Asp His His Gln Val				
1280		1285		1290
Tyr Ala Ala Ser Phe Ser Cys Pro Glu Gly Thr Thr Phe Gly Ser				
1295		1300		1305
Gln Cys Ser Phe Gln Cys Arg His Pro Ala Gln Leu Lys Gly Asn				
1310		1315		1320
Asn Ser Leu Leu Thr Cys Met Glu Asp Gly Leu Trp Ser Phe Pro				
1325		1330		1335
Glu Ala Leu Cys Glu Leu Met Cys Leu Ala Pro Pro Pro Val Pro				
1340		1345		1350
Asn Ala Asp Leu Gln Thr Ala Arg Cys Arg Glu Asn Lys His Lys				
1355		1360		1365
Val Gly Ser Phe Cys Lys Tyr Lys Cys Lys Pro Gly Tyr His Val				
1370		1375		1380
Pro Gly Ser Ser Arg Lys Ser Lys Lys Arg Ala Phe Lys Thr Gln				
1385		1390		1395
Cys Thr Gln Asp Gly Ser Trp Gln Glu Gly Ala Cys Val Pro Val				
1400		1405		1410
Thr Cys Asp Pro Pro Pro Pro Lys Phe His Gly Leu Tyr Gln Cys				
1415		1420		1425

Thr Asn Gly Phe Gln Phe Asn Ser Glu Cys Arg Ile Lys Cys Glu
1430 1435 1440

Asp Ser Asp Ala Ser Gln Gly Leu Gly Ser Asn Val Ile His Cys
1445 1450 1455

Arg Lys Asp Gly Thr Trp Asn Gly Ser Phe His Val Cys Gln Glu
1460 1465 1470

Met Gln Gly Gln Cys Ser Val Pro Asn Glu Leu Asn Ser Asn Leu
1475 1480 1485

Lys Leu Gln Cys Pro Asp Gly Tyr Ala Ile Gly Ser Glu Cys Ala
1490 1495 1500

Thr Ser Cys Leu Asp His Asn Ser Glu Ser Ile Ile Leu Pro Met
1505 1510 1515

Asn Val Thr Val Arg Asp Ile Pro His Trp Leu Asn Pro Thr Arg
1520 1525 1530

Val Glu Arg Val Val Cys Thr Ala Gly Leu Lys Trp Tyr Pro His
1535 1540 1545

Pro Ala Leu Ile His Cys Val Lys Gly Cys Glu Pro Phe Met Gly
1550 1555 1560

Asp Asn Tyr Cys Asp Ala Ile Asn Asn Arg Ala Phe Cys Asn Tyr
1565 1570 1575

Asp Gly Gly Asp Cys Cys Thr Ser Thr Val Lys Thr Lys Lys Val
1580 1585 1590

Thr Pro Phe Pro Met Ser Cys Asp Leu Gln Gly Asp Cys Ala Cys
1595 1600 1605

Arg Asp Pro Gln Ala Gln Glu His Ser Arg Lys Asp Leu Arg Gly
1610 1615 1620

Tyr Ser His Gly
1625